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Use of Pure Boswellia Acid

[Verwendung von reiner Boswelliasäure]

Prof. Dr. P.T. Hermann Ammon et al.

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Inventors	:	Prof. Dr. P.T. Hermann Ammon, Dr. Chem. Hasan Safayhi and Dr. Chem. G.B. Singh
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This invention relates to the use of pure Boswellia acid, a physiologically acceptable salt, a derivative, a salt of the derivative or a plant preparation containing Boswellia acid for the prevention and/or fight against inflammatory processes that are triggered by increased leukotrienes in human or veterinary medicine.

The invention also relates to the pure of Boswellia acid or a physiologically accepted salt, a derivative, a salt of the derivative or a plant preparation containing Boswellia acid for the production of a medication for the treatment of inflammatory processes caused by increased formation of leukotrienes in human or veterinary medicine.

According to the invention, this substance is used especially for inflammatory joint diseases, epidermal lesions (psoriasis), allergic or chromic asthma, endotoxin shock, inflammatory intestinal diseases (Colitis ulcerosa, Morbus Crohn) and chronic hepatitis.

Inflammatory reactions are measures of the organism intended after a tissue has been damaged to remove the foreign body that causes the damage or the damaged part of the tissue and replace it with repaired tissue. An inflammation is thus a

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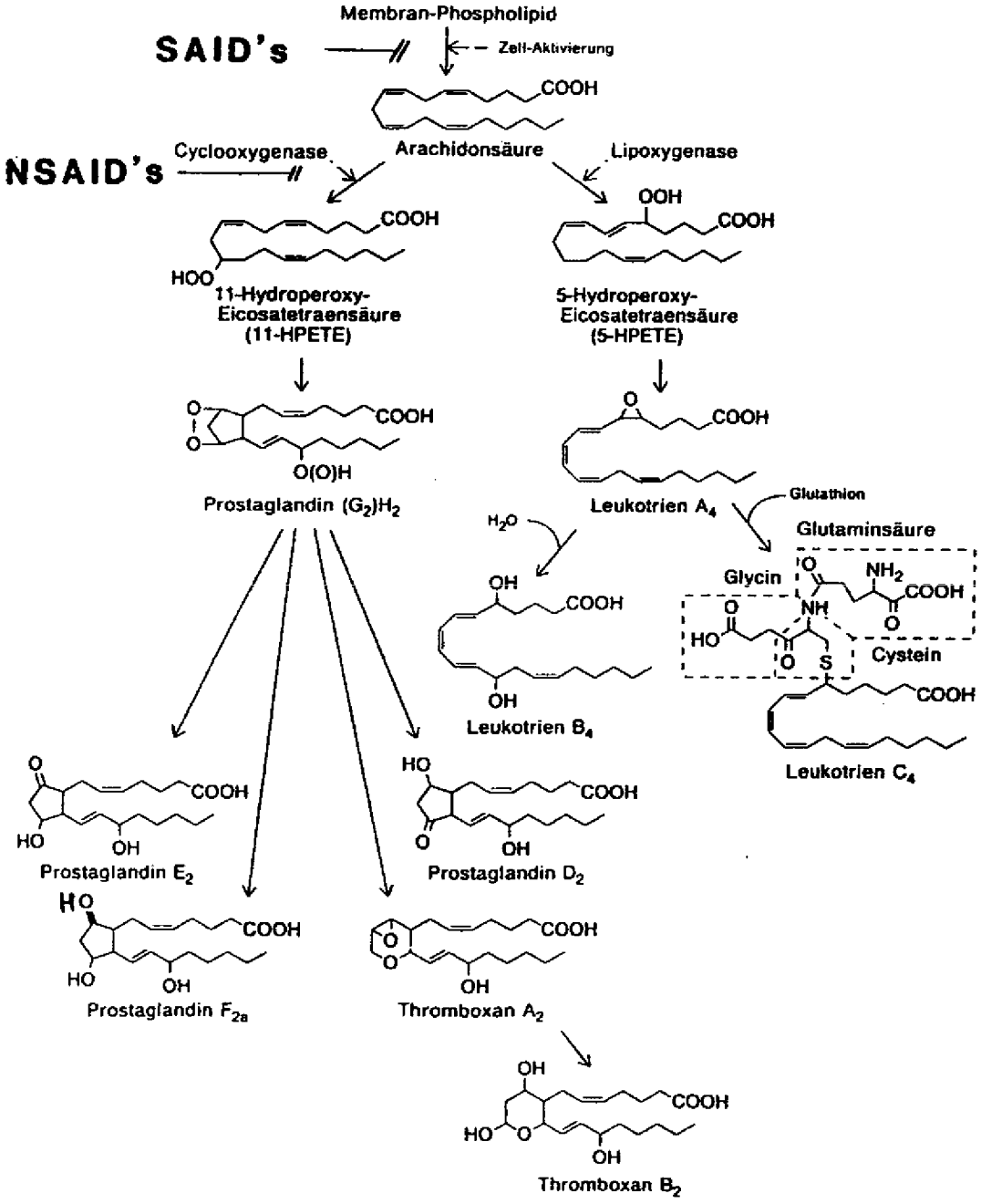
[1] Numbers in the margin indicate pagination in the foreign text.

physiological process. But there are a series of situations where inflammatory processes can control additional functions of organs that must then be subjected to therapeutic measures. Important inflammations take place, for example, in the region of the joints (rheumatism), in the region of the bronchia and in the region of the entire gastrointestinal tract. Use of substances that inhibit the inflammation are one way used by present-day therapy to eliminate inflammations.

Inflammations are triggered biochemically due to the release of so-called inflammation mediators. The following play a role as such: prostaglandins, leukotrienes, histamines, bradyquinine and complementary factors.

The synthesis of prostaglandins and leukotrienes takes place at the site of inflammation according to the following scheme:



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[Key: 1) Membran = membrane; 2) Zell-aktivierung = cell activation; 3) Arachidonsäure = arachidonic acid; 4) Eicosatetraensäure = eicosatetraenic acid; 5) Glutaminsäure = glutaminic acid].

This scheme shows that there are two essential types of inflammation mediators that are involved in the genesis and maintenance of inflammations: prostaglandins and leukotrienes.

Prostaglandins perform the following functions during the event of inflammation: changes in the vascular tone, increase in vascular permeability, triggering of pain, regulation of coagulation processes and of stomach juice secretion, fever. Leukotrienes cause a contraction of the blood vessel (arteries) and the bronchia, an increase in vascular permeability (discharge of edema fluid) and the specifically targeted enticement of leukocytes (see Forth/Henschler/Rummel, General and Special Pharmacology and Toxicology, 5th edition, 1987, pp. 176 to 214 and 522 to 546).

Today, medications are used in the treatment of inflammation; these medications are mostly in a position to block the so-called arachidonic acid cascade, specifically the part that leads to the formation of the prostaglandins by inhibiting the enzyme cyclooxygenase. The most important /4 of these inhibiting substances are: acetylsalicylic acid and derivatives of other weak carboxylic acids, pyrazolone derivatives and aminophenols.

Among these substances that are used as antiphlogistics (NSAID's = nonsteroidal antirheumatics), however, only the left

part of this cascade but not also the part of the cascade that leads to the formation of leukotriene can be influenced.

The place where these substances attack is marked "NSAID's" in the abovementioned diagram. These nonsteroidal antirheumatics thus have no or almost no effect in relation to inflammatory processes where leukotrienes are formed.

The other possibility of treating inflammations is to use glucocorticoids, in particular, cortisone. The glucocorticoids are referred to as "SAID's = steroidal antirheumatics, and they inhibit the formation of phospholipase A2. The above diagram shows the spot where the steroidal antirheumatics attack. One can readily see that they block both parts of the arachidonic acid cascade, that is to say, on the one hand, they inhibit the formation of prostaglandin and, on the other hand, they inhibit the formation of leukotrienes. In many diseases where leukotriene is formed, such as, for example, in inflammatory joint diseases, epidermal lesions (psoriasis) and allergic and chronic asthma as well as inflammatory intestinal diseases, however, corticoids must be administered over a longer period of time. The well-known side effects on the metabolism and the hormone systems constitute a big problem in the long-term use of corticoids; these effects are manifested, among other things, also by the symptoms of Morbus Cushing. Other side effects are the moon-shaped face, essential obesity, muscle weakness,

hypertonia, osteoporosis, stomach complaints and the obstruction of immune processes, just to mention a few. The use of glucocorticoids is confined to emergency situations. Glucocorticoids, therefore, are unsuitable for long-term use.

So far there is not a single substance in therapy that is capable of influencing the inflammation event in a selective manner on the side of leukotriene synthesis inhibition. The availability of such substances would constitute considerably therapeutic progress. Many institutes throughout the world therefore are looking for such substances now. A series of such substances were found, but in all of them, it was discovered that they are too toxic to be considered for therapy.

The Ayurvedic medicine of India employs medications that contain preparations from the plant Boswellia serrata for the treatment of inflammations but also for rheumatism. In the past, it has not yet been known, above all it has not been documented scientifically, which of the constituents of this medicinal plant exercises the antiphlogistic effect. In particular, it was not known how the extracts that are used take effect and these medications were used primarily for diseases where the prostaglandins are formed as inflammation mediators. The use of these medications in diseases were leukotrienes are formed is not described in the literature.

In the case of Morbus Crohn, we are dealing with two chronically inflammatory intestinal diseases that cannot be influenced or that can be influenced only inadequately with the currently available therapy. Looking at it from the viewpoint of pathological physiology, it is assumed that excessive formation of so-called leukotrienes (inflammation mediators that, in particular, serve as attractants for white blood cells) are the main cause for the fact that these diseases keep occurring. So far, there is practically no effective medication against inflammatory intestinal diseases. We do, of course, have available so-called glucocorticoids (derivatives of adrenal cortex hormones), in particular, cortisone. But, as noted above, they feature considerable side effects so that their use is not unproblematical. The use of sulfasalazine is also unsatisfactory. Sulfasalazine is a substance that mostly inhibits the formation of so-called prostaglandins (also inflammation mediators). But by preventing the synthesis of prostaglandins, we cannot always attain the goal in the treatment of these diseases.

Chronic asthma and psoriasis are diseases for which there are so far no satisfactorily effective medications. Both diseases are treated, among other things, with cortisone or cortisone derivatives. The administration of cortisone and its derivatives, especially over a longer period of time, however,

is connected with considerable disadvantages. Chronic hepatitis likewise cannot be treated in a satisfactory manner.

The object of the invention at hand is to provide the use of preparations that serve for the prevention of and/or fight against diseases that are accompanied by excessive generation of leukotrienes. The preparation available according to the invention is intended to be able to influence the inflammation event selectively in terms of leukotriene synthesis inhibition. The invention, in particular, is intended to show a way of replacing the steroidal antirheumatics; possibilities are to be provided according to which one can over a longer period of time administer a medication that inhibits leukotriene synthesis without any side effects and especially the side effects of /5 of the steroidal antirheumatics. According to the invention, the use of a medication is to be made available, which can be used for chronic inflammatory diseases and which takes effect especially in connection with inflammatory joint disease, epidermal lesions (psoriasis), allergic and chronic asthma, endotoxin shock, inflammatory intestinal diseases (Colitis ulcerosa, Morbus Crohn) and chronic hepatitis. The medication, made available according to the invention, is to be nontoxic and is to be well tolerated by the patients. The pharmaceutical industry is feverishly looking for leukotriene synthesis

inhibitors that are nontoxic, especially for the treatment of the diseases mentioned.

It was now found quite surprisingly that Boswellia acid, a physiologically acceptable salt, a derivative, a salt of the derivative or a plant preparation containing Boswellia acid, acts to prevent and/or fight inflammatory processes that are triggered by increased leukotriene formation in human or veterinary medicine.

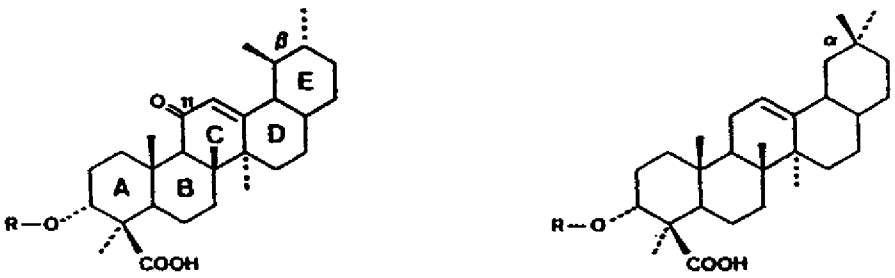
With the help of the test with calcium and ionophoric-stimulated neutrophile leukocytes of the rat, it was possible to prove that extracts from Boswellia serrata primarily block the formation of leukotrienes, whereas prostaglandin synthesis is influenced only at considerably higher concentrations (see regarding the methodology: a) "Measurement of Leukotrienes," Safayhi et al., Biochem. Pharmacology, 34:2691-2694, 1985; b) "Measurement of Prostaglandins: Commercial Radio-Immunoassay Kits by the Amersham Company for 6-Keto-PGF1α").

The plant Boswellia serrata must therefore have constituents that precisely are in a position somewhat selectively to inhibit the arachidonic acid cascade in terms of leukotriene formation. According to the data provided by Pardhy & Bhattacharyya (Ind. J. Chem., 16B:176-178, 1978), Boswellia serrata essentially contains the following constituents: β-Boswellia acid, acetyl-β-boswellia acid, acetyl-11-keto-β-

boswellia acid, 11-keto-β-boswellia acid on which, however, so far there are no pharmacological investigations in the area of prevention of inflammation. On the basis of the information provided in the bibliographic entry by G.B. Singh and C.K. Atal, "Agents and Actions," Vol. 18, p. 410, one should have expected that Boswellia acid does not have any effect on inflammations that are caused by leukotrienes. On p. 410, right-and column, this bibliographic reference states that Salai guggal, an extract obtained from Boswellia serrata, has no effect with relation to the cotton-pellet-induced granuloma test that is characteristic for the abovementioned SAID's medications.

The structural formulas for Boswellia acid and some of its derivatives are given below:

(A):



R = H : 11-keto-β-boswellia acid

R = acetyl: acetyl-11-keto-β-boswellia acid

R = formyl: formyl-11-keto-β-boswellia acid

(B):

[Please insert formula on original page 6]. /6

R = H : α-boswellia acid

R = acetyl: acetyl-α-boswellia acid

R = formyl: formyl-α-boswellia acid

As Boswellia acid, one preferably uses β-boswellia acid that, according to bibliographic data, is isolated from Boswellia serrata or other known plants containing Boswellia acid. β-boswellia acid can contain small quantities of α- or β-boswellia acid. The sodium, potassium, ammonium and calcium salts can be used as physiologically acceptable salts of Boswellia acid. As derivatives of Boswellia acid, one can use lower alkyl esters that are obtained by means of the esterification of the carboxyl group with a C_1-C_6-alcohol, preferably methyl ester or ester that is obtained by the esterification of the hydroxyl group with a physiologically tolerable carboxylic acid. Preferred derivatives are β-boswellia acid acetate, β-boswellia acid formiate, β-boswellia acid methyl ester, acetyl-β-boswellia acid, acetyl-11-keto-β-boswellia acid and 11-keto-β-boswellia acid.

According to the invention, it was furthermore possible to use a plant preparation containing Boswellia acid. Preparations contained from the resin are used according to the invention.

Plants that contain Boswellia acid (synonym: Boswellin acid) are as follows:

Boswellia (serrata, papyrifera, frereana, carteri, thurifera, glabra, bhaw-dajiana, oblongata, socotrana and other representatives of that family), primarily the resin.

According to the invention, it is furthermore possible to use them together with other chemically pure medicinal substances and/or plant medications. Here are examples of such other chemically pure medicinal substances:

BRONCOLYTICS AND ANTIASTHMATICS

SYMPATHOMIMETICS:

- Carbuterol-HCl
- Clenbuterol-HCl
- Fenoterol-HBr
- Isoetarin-HCl
- Orciprenalin sulfate
- Pirbuterol-HCl
- Procaterol-HCl
- Reproterol-HCl
- Sabutamol sulfate
- Terbutalin sulfate
- Tulobuterol-HCl

ANTIPSORIATICS

NONSTEROIDAL ANTIPHLOGISTICS:

- Salicylic acid and derivatives

VITAMINS:

- Folic acid
- Vitamin E
- Vitamin B12 /7
- Vitamin B

MISCELLANEOUS:

- Cadmium sulfide
- Benzalkonium chloride
- Sodium bitumen sulfonate
- Ammoidine
- Allantoin
- Methotrexate
- Paraffin
- Tioxolone
- Dithranol
- Fumaric acid
- Undecylenic acid
- Polyoxyethylene lauryl ether sulfate
- Etretinate
- Zinc oxide
- Urea
- Lactic acid

NONSTEROIDAL ANTIRHEUMATICS:

- Azapropazone
- Bumadizone

- Famprofazone
- Mofebutazone
- Nifenazone
- Oxyphenbutazone
- Phenylbutazone
- Pyrazinobutazone

ARYLACETIC ACID DERIVATIVES AND INDOLE DERIVATIVES:

- Acemetacine
- Bufexamac
- Diclofenac
- Indometacin
- Lonazolac
- Proglumetacin
- Tolmetin

ANTHRANILIC ACID DERIVATIVES:

- Flufenaminic acid
- Mefenaminic acid
- Nifluminic acid

ARYLPROPIONIC ACID DERIVATIVE:

- Carprofen
- Fenoprofen
- Fenbufen
- Flurbiprofen
- Ibuprofen

- Ketoprofen /8
- Naproxen
- Piroxicam
- Pirprofen
- Tiaprofenic acid

OXICAMS:

- Tenoxicam

MISCELLANEOUS:

- Benzydamine
- Benfotiamine
- Chloroquine
- Hydroxychloroquine
- Auranofine
- (1-D-glucosylthio)gold
- Aurothiomalate
- Aurothiopolypeptide
  (= gold keratinate)
- Tetrachlorogold(III) acid
- D-penicillamin
- Hyaluronidase
- Nabumeton
- Etofenamate
- Ademetionine
- Serrapeptase

- Azathioprine
- Chlorambucil
- Cyclophosphamide
- Methotrexate
- Glucosamine sulfate
- Penicillin
- Bienengift preparation
- Sulfur
- Oxaceprol
- Orgoteine
- Sulfasalazine

  (= Salazosulfapyridine)

Boswellia acids inhibit the activity of 5-lipoxygenase and thus the generation of inflammation mediators of the leukotriene type. They inhibit 5-lipoxygenase, specifically, that is to say, neither 12-lipoxygenase (12-HETE formation) nor cyclooxygenase activity (prostanoid formation) are impaired by Boswellia acid. In contrast to the many experimentally employed 5-lipoxygenase inhibitors (for example, NDGA, BW755c, etc.), which, due to their reducing effect, could potentially nonselectively inhibit all oxidizing enzymes, the Boswellia acids do not have any reducing properties. Such a specific inhibitor of 5-lipoxygenase that due to its high selectivity also seems suitable for in-vivo parenteral administration in the

case of diseases mediated by leukotriene is not available on the market.

The following illustration will elucidate the attack site and action mechanism of the Boswellia acids:

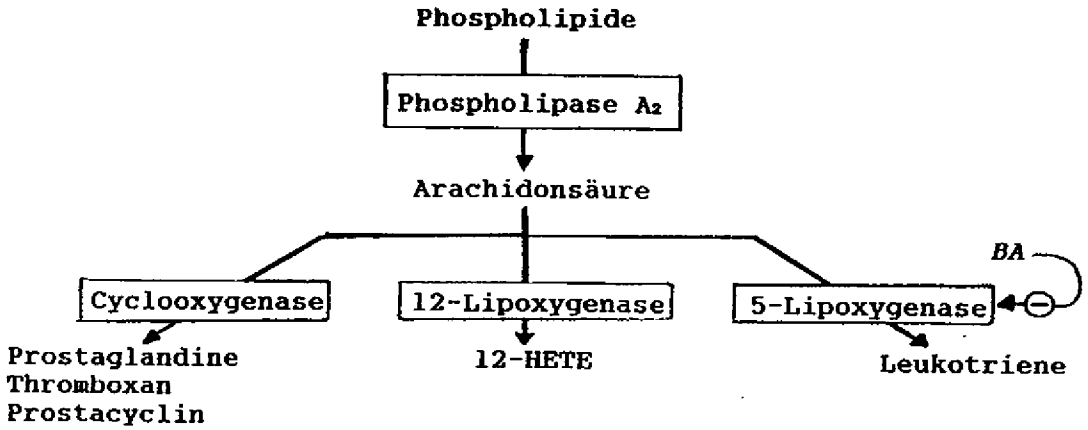


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TABLE: Inhibition of 5-Lipoxygenase by Boswellia Acids

[Key: 1) Arachidonsäure = arachidonic acid].

The following Boswellia acids (syn.: Boswellin acids) or derivatives were isolated and displayed a 5-lipoxygenase-inhibiting effect:

Boswellia acids	IC_{50} Values for 5-LO-inhibition (µM)
β-Boswellia acid	5
Acetyl-boswellia acid	7
11-keto-β-boswellia acid	5
Acetyl-11-keto-β-boswellia acid	2

α-Boswellia acid	5
Acetyl-α-Boswellia acid	7

The invention will now be explained in greater detail with reference to the attached drawings.

Fig. 1 shows 5-lipoxygenase activity in isolated, stimulated, neutrophile granulocytes from the peritoneum of the rat in the presence of rising concentrations of acetyl-11-keto-β-Boswellia acid (●), nordihydroguaiaretic acid (■) and hydrocortisone (▲). Method: Safayhi, Tiegs, Wendel, 1985.

Fig. 2 shows the 12-lipoxygenase activity in isolated, stimulated thrombocytes of man in the presence of rising concentrations of acetyl-boswellia acid (●), nordihydroguaiaretic acid (■) and indometacine (□). Method: Safayhi et al., JPET accepted.

Fig. 3 shows the cyclooxygenase activity in isolated, stimulated thrombocytes of man in the presence of rising concentrations of acetyl-boswellia acid (●), nordihydroguaiaretic acid (■) and indometacine (□). Method: Safayhi et al., JPET accepted.

Fig. 4 shows the elutions profiles of the oxidized and hydroxylated products generated due to iron/ascorbate stimulation from exogenous arachidonic acid in the cell-free system in the presence of rising concentrations of acetyl-

boswellia acid (A) and nordihydroguaiaretic acid (B). Method: Safayhi et al., JPET accepted.

All diseases that are accompanied by the formation of leukotriene can be treated according to the invention. But it is preferable to treat, as inflammations, inflammatory joint diseases, epidermal lesions (psoriasis), allergic and chronic asthma, endotoxin shock and inflammatory intestinal diseases such as Colitis ulcerosa and Morbus Crohn and chronic hepatitis.

According to the invention, Boswellia acid is used as /10 required. Because it is little toxic, the dosage is not critical and can be varied easily by the doctor as a function of the seriousness of the disease, the weight of the patient to be treated and the duration of treatment.

Standard doses can, for example, be administered one to four times per day. The exact dose depends on the administration route and the condition that is to be treated. Naturally, it may be required to perform routine variations of the dose, depending on the age and weight of the patient as well as the seriousness of the pathological state to be treated.

The preparations to be used according to the invention can be formulated in the known manner using one or several pharmaceutically acceptable carriers or diluents. The preparations can be formulated for oral, parenteral, rectal or intranasal administration or in a manner suitable for

administration by inhalation or insufflation. Preparations of the compounds for oral administration are preferred.

The pharmaceutical preparations for oral administration can assume the form, for example, of tablets or capsules that are present according to known methods with pharmaceutically acceptable diluents such as bonding agents (for example, pregelatinized cornstarch, polyvinylpyrrolidone or hydroxypropylmethylcellulose); fillers (for example, lactose, saccharose, mannite, corn starch, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (for example, stearic acid, polyethylene glycol, magnesium stearate, talc or silicon dioxide); disintegration agents (for example, potato starch, sodium starch glycolate or sodium carboxymethylcellulose); wetting agents (for example, sodium lauryl sulfate). The tablets can be coated in accordance with known methods. Liquid preparations for oral administration can be present in the form, for example, of aqueous or oleaginous solutions, syrups, elixirs, emulsions or suspensions, or they can be present as dry product for constitution with water or some other suitable carrier prior to actual use. Such liquid preparations can be made by means of known methods with pharmaceutically acceptable additives such as suspension agents (for example, sorbite syrup, cellulose derivatives, glucose/sugar syrup, gelatins, aluminum stearate gel or hydrated consumable fats); emulsifiers (for

example, lecithin, Gummi arabicum or Sorbitan monooleate); nonaqueous carriers (for example, almond oil, oily esters, ethyl alcohol or fractionated vegetable oils) and conservation agents (for example, methyl- or propyl-p-hydroxybenzoates or sorbic acid). The liquid preparations can also contain known buffers, taste or aromatic agents, dyes and sweeteners, as needed.

For parenteral administration, the compounds can be formulated for injection, preferably intravenous, intramuscular or subcutaneous injection. Preparations for injection can be single-dose form, for example, in ampules, or in multi-dose containers with an added conservation agent. The preparations can be present in the form of suspensions, solutions or emulsions in oily or aqueous carriers and can contain adjuvants such as suspension, stabilizing and/or dispersion agents and/or means for setting the tonicity of the solution. As an alternative, the active component can be present in the form of a powder for constitution with a suitable carrier, for example, sterile pyrogen-free water prior to use.

The compounds can also be formulated as rectal preparations such as suppositories, for example, those that contain known basic suppository substances such as cocoa butter or other glycerides.

For intranasal administration, the compounds can be used as liquid sprays in the form of drops or as snuffing powder.

For purposes of administration by way of inhalation, the compounds in a practical supplied in the form of an aerosol spray from a pressurized package using suitable propellants or in an atomizer device. If the aerosol is under pressure, the dose unit will be determined in that a valve is provided that releases a measured quantity. Capsules and cartridges, for example, made of gelatins for use in an inhalation device or an insufflation device can be so prepared that they will contain a powder mixture made up of an invention-based employed compound and a suitable basic powder substance such as lactose or starch.

The following examples will explain the invention-based manner of use.

Example 1 /11

Tablets for Oral Administration

A. Direct Compression

Active substance: Boswellia acid	15-30 mg/tablet
(or pulverized drug)	0.5 - 1.0 g/tablet
Magnesium stearate BP	0.65 mg/tablet
Anhydrous lactose	80 mg/tablet

The active substance is mixed with anhydrous lactose and magnesium stearate and the mixture is screened. The resultant mixture is pressed to make tablets using a tabletting machine.

Active substance: Boswellia acid	15-30 mg/tablet
(or pulverized drug)	0.5 - 1.0 g/tablet
Magnesium stearate BP	0.7 mg/tablet

Microcrystalline cellulose NF	100 mg/tablet

The active substance is screened and is mixed with the microcrystalline cellulose and the magnesium stearate. The resultant mixture is pressed into tablets using a tabletting machine.

B. Wet Granulation

Active substance: Boswellia acid	15-30 mg/tablet
(or pulverized drug)	0.5 - 1.0 g/tablet
Lactose BP	150.0 mg/tablet
Starch BP	30.0 mg/tablet
Pregelatinized cornstarch BP	15.0 mg/tablet
Magnesium stearate BP	1.5 mg/tablet

The active substance is run through a suitable screen and is mixed with lactose, starch and pregelatinized cornstarch. One adds suitable volumes of purified water and the powder is then granulated. After drying, the granulate is run through a screen and is mixed with magnesium stearate. The granulate is then pressed into tablets using perforate punches with a suitable diameter.

Tablets with different composition can be made in that one changes the ratio between active substance and lactose or the compression weight and uses corresponding perforation punches.

Example 2

Capsules	
Active substance: Boswellia acid	15-30 mg/capsule
(or granulated drug)	0.5 - 1.0 g/capsule
Free-flowing starch	150.00 mg/capsule

Magnesium stearate BP	1.00 mg/capsule

The active substance is run through a screen and is /12 mixed with the other constituents. The mixture is filled into hard gelatin capsules using a suitable device. Other capsules can be made in that one alters the charging weight and that one changes the size of the capsule accordingly, if required.

Example 3

Syrup

Saccharose-free preparation		mg/5 ml dose
Active substance: Boswellia acid		15 - 30
Hydroxypropylmethylcellulose USP (Viscosity type 4000)		22.5
Buffer	)	
Flavoring substance	)	
Dye	}	as needed
Conservation agent	}	
Sweetening agent	}	
Purified water	to	5.0 ml

Hydroxymethylcellulose is dispergated in hot water, it is cooled down and it is then mixed with an aqueous suspension that contains the active substance and the other components of the preparation. The resultant solution is then adjusted for its volume and mixed.

Example 4

Suspension		mg/5 ml dose
Active substance: Boswellia acid		15 - 30
(or pulverized drug)		0.5 - 1.0 g)
(dried drug extract accordingly)		
Aluminum monostearate		75.00
Sweetening agent	)	
Flavoring agent	)	as needed
Dye	)	
Fractionated coconut oil	to	5.00

The aluminum monostearate is dispergated in about 90% of the fractionated coconut oil. The resultant suspension is heated while stirring to 115°C and is then cooled down. One then adds the sweetening agents, the flavoring agents and the dyes and the active substance is dispergated. The suspension is set for volume with the remaining fractionated coconut oil and is mixed.

Example 5 /13

Sublingual tablet	
Active substance: Boswellia acid	15-30 mg/tablet
(or drug extract)	0.5 - 1.0 g/tablet
Pressable sugar NF	50.5 mg/tablet
Magnesium stearate BP	0.5 mg/tablet

The active substance is run through a suitable screen, it is mixed with the other constituents and it is pressed using

suitable perforation punches. Tablets of other thickness can be made in that one changes the ratio between active substance and carrier or the compression rate.

Example 6

Suppositories for rectal administration	
Active substance: Boswellia acid	15-30 mg
Witepsol H15[+] to	1.0 g

+ suitable quality of Adeps solidus Ph.Eur.

A suspension of the active substance in melted Witepsol is made and is charged into 1-g suppository molds using a suitable device.

Example 7

Injection for intravenous administration	
Active substance: Boswellia acid	15-30 mg/ml
Sodium chloride intravenous infusion BP, 0.9% weight/volume to	1 ml
Preparation size 2,500 ml	

The active substance is dissolved in a part of the sodium chloride intravenous infusion, the solution is set for the volume with the sodium chloride intravenous infusion and the solution is thoroughly mixed. The solution is charged into clear, Type 1, 10-ml glass ampules and it is sealed off under nitrogen in the head area by melting off the glass. The ampules are sterilized by heating in the autoclave at 120°C for no less than 20 minutes.

Example 8

Cartridge for inhalation

Active substance (micronized): Boswellia acid	15-30 mg/cartridge
Lactose BP	25.00

The active substance is micronized in a jet mill to form a fine particle size range and is then mixed with lactose. The powder mixture is charged into No. 3 hard gelatin capsules.

Example 9 /13

Nasal Spray

Active substance: Boswellia acid		1.5 - 3.0 %/vol.
Conservation agent	)	as needed
Sodium chloride BP	)	
Purified water BP	to	100
Dispensing weight		100 mg (equivalent to 7 mg active substance)

The active substance, the conservation agent and the sodium chloride are dissolved in a part of the water. The solution is set to volume with water and the solution is thoroughly mixed.

Claims

1. Use of pure Boswellia acid, a physiologically acceptable salt, a derivative, a salt of the derivative or a plant preparation containing Boswellia acid for the prevention and/or fight against inflammatory processes that are triggered by increased leukotrienes in human or veterinary medicine.

2. Use according to Claim 1, **characterized in** that this substance is used especially for inflammatory joint diseases, epidermal lesions (psoriasis), allergic or chromic asthma, endotoxin shock, inflammatory intestinal diseases (Colitis ulcerosa, Morbus Crohn) and chronic hepatitis.

3. Use according to one of Claims 1 or 2, **characterized in** that the method of use is intraperitoneal, oral, buccal, rectal, intramuscular, topical, subcutaneous, intraarticular or intravenous.

4. Use according to one of Claims 1, 2 or 3, **characterized in** that use involves the form of tablets, coated tablets, capsules, solutions, emulsions, ointments, creams, inhalation preparations, aerosols or suppositories.

5. Use of pure Boswellia acid or a physiologically accepted salt, a derivative, a salt of the derivative or a plant preparation containing Boswellia acid for the production of a medication for the treatment of inflammatory processes caused by increased formation of leukotrienes in human or veterinary medicine.

6. Use according to Claim 5, **characterized in** that a medication is made for the treatment of inflammatory joint diseases, epidermal lesions (psoriasis), allergic or chronic asthma, endotoxin shock, inflammatory intestinal

diseases (Colitus ulcerosa, Morbus Crohn) and chronic hepatitis.

7. Use according to one of Claims 5 or 6, **characterized in** that the substance is used for the production of a medication for intraperitoneal, oral, buccal, rectal, intramuscular, topical, subcutaneous, intraarticular or intravenous administration.

8. Use according to one of Claims 5, 6 or 7, **characterized in** that it is used for the production of a medication in the form of tablets, coated tablets, capsules, solutions, emulsions, ointments, creams, inhalation preparations, aerosols or suppositories.

9. Use according to at least one of Claims 1 to 8, /15 **characterized in** that the substance is used together with other chemically pure medicinal substances/or plant medications.

FIG. 1

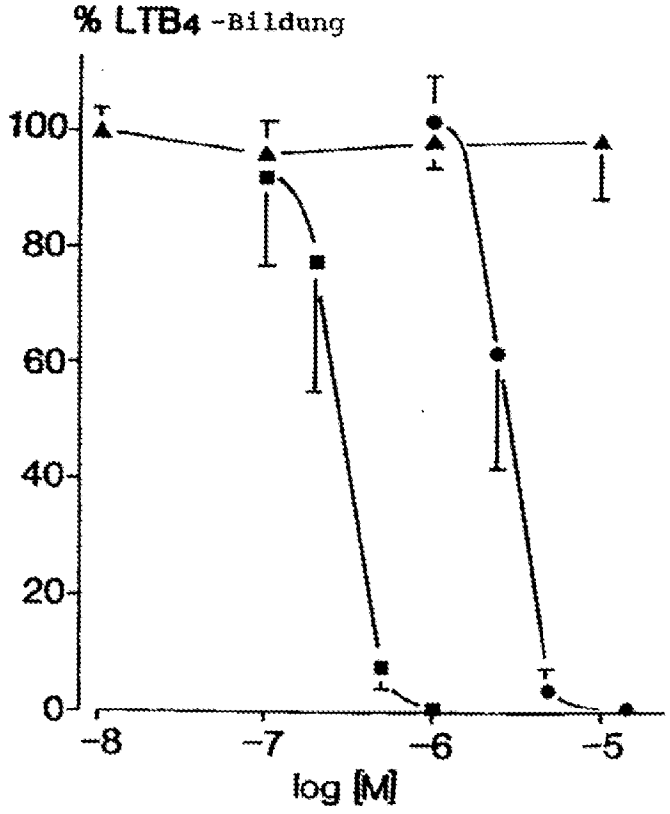


FIG. 2

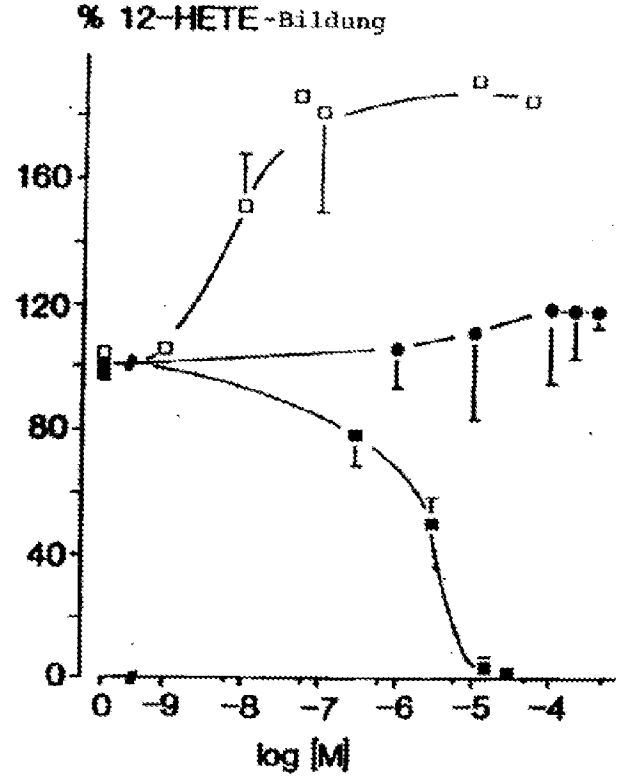
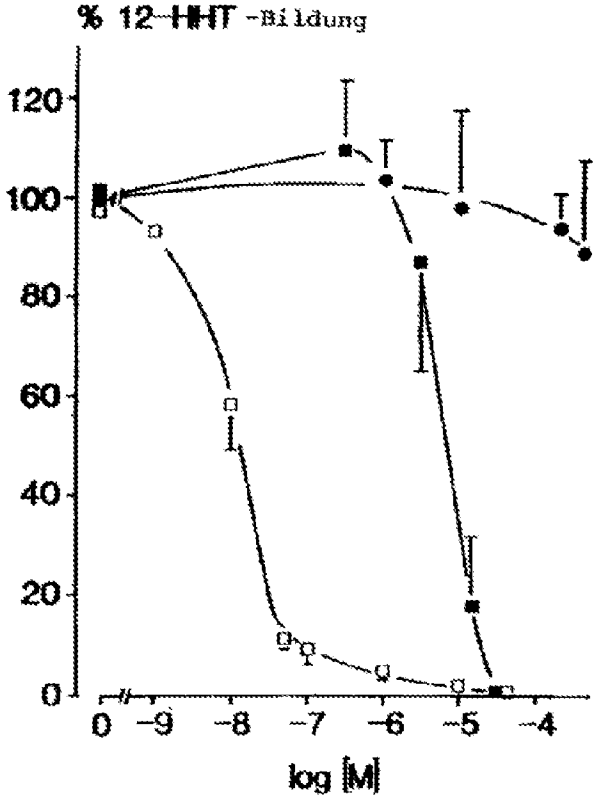
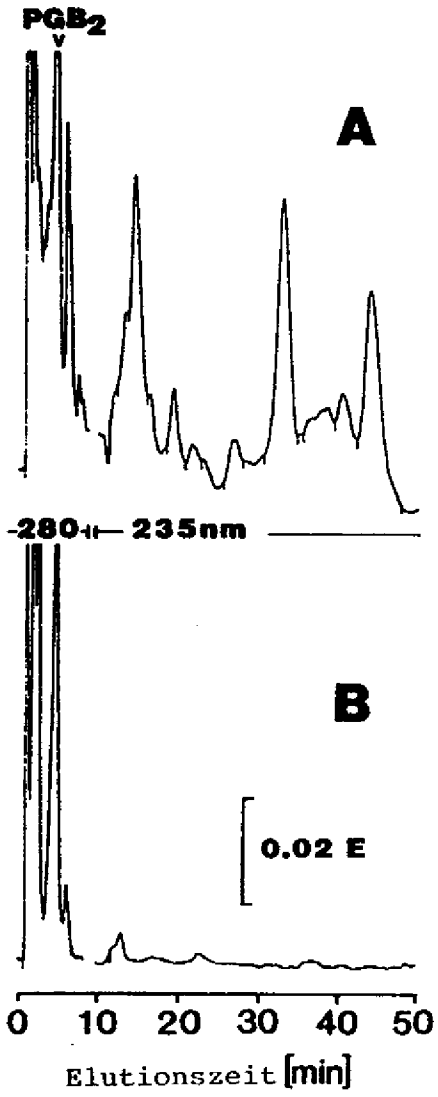

% 12-HETE-Bildung
160
120
80
40
0
0 -9 -8 -7 -6 -5 -4
log [M]

FIG. 3


% 12-HHT -Bildung
120
100
80
60
40
20
0
0 -9 -8 -7 -6 -5 -4
log [M]

[Key: 1) Bildung = Formation].

FIG. 4



[Key: 1) Elutionszeit = Elution time].